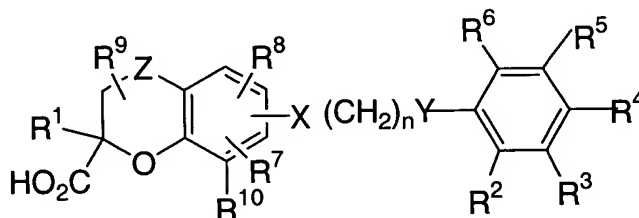


## Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in this application.

### Listing of Claims

1. (Currently Amended) A compound having the formula I:



or a pharmaceutically acceptable salt or prodrug thereof, wherein:

Z is selected from the group consisting of CH<sub>2</sub> and C=O;

R<sup>1</sup> is selected from the group consisting of Cl, Br, F and C<sub>1-4</sub> alkyl, wherein said C<sub>1-4</sub> alkyl is linear or branched and is optionally substituted with 1-3 halogens independently selected from F and Cl, 1 phenyl which is optionally substituted with 1-3 halogens, or a mixture thereof; H, OH, C<sub>1-7</sub> alkyl, C<sub>2-7</sub> alkenyl, C<sub>2-7</sub> alkynyl, OC<sub>1-3</sub> alkyl, OC<sub>2-3</sub> alkenyl, OC<sub>2-3</sub> alkynyl, F, Br, Cl, and Ar, wherein alkyl, alkenyl, alkynyl, Oalkyl, Oalkenyl and Oalkynyl are linear or branched and are optionally substituted with (a) 1-7 halogen atoms, (b) 1-3 groups independently selected from (i) OC<sub>1-3</sub> alkyl, which is optionally substituted with 1-5 halogen atoms, and (ii) phenyl, which is optionally substituted with 1-3 groups independently selected from halogen, C<sub>1-5</sub> alkyl and OC<sub>1-3</sub> alkyl, said C<sub>1-</sub>

~~5alkyl and -OC<sub>1-3</sub>alkyl being linear or branched and optionally substituted with 1-5 halogens, or (c) a mixture of (a) and (b);~~

Ar is Aryl, wherein Aryl is in each instance optionally substituted with 1-5 substituents independently selected from (a) halogen, (b) C<sub>1-5</sub>alkyl, (c) C<sub>2-5</sub>alkenyl, (d) C<sub>2-5</sub>alkynyl, (e) -OC<sub>1-5</sub>alkyl, (f) -OC<sub>2-5</sub>alkenyl, (g) -OC<sub>2-5</sub>alkynyl, (h) -SO<sub>x</sub>C<sub>1-5</sub>alkyl, (i) -SO<sub>x</sub>NR<sup>a</sup>R<sup>b</sup>, (j) -SO<sub>x</sub>phenyl, (k) -C(O)C<sub>1-3</sub>alkyl, and (l) -C(O)NR<sup>a</sup>R<sup>b</sup>, wherein in each instance, each alkyl, alkenyl and alkynyl is linear or branched and is optionally substituted with (a) 1-5 halogen atoms, (b) 1-2 groups independently selected from -OC<sub>1-3</sub>alkyl, which is linear or branched and is optionally substituted with 1-5 halogens, or (c) a mixture thereof, and wherein phenyl is optionally substituted with 1-3 substituents independently selected from halogen, C<sub>1-3</sub>alkyl, and C<sub>1-3</sub>alkoxy, wherein C<sub>1-3</sub>alkyl and C<sub>1-3</sub>alkoxy are linear or branched and are optionally substituted with 1-5 halogens;

x is selected from 0, 1 and 2;

Aryl is a carbocyclic 6-10 membered monocyclic or bicyclic aromatic ring system;

Hetcyc is a 5- or 6-membered saturated or partly saturated monocyclic heterocycle having 1-4 heteroatoms independently selected from N, S, and O in the perimeter of the ring, wherein N may optionally be NR<sup>a</sup> and S may optionally be SO or SO<sub>2</sub>;

Benzoheterocycle comprises a 5 or 6-membered heterocyclic ring which may be saturated, partly unsaturated or aromatic, and a benzene ring, wherein said heterocyclic ring and said benzene ring are fused together, wherein said heterocyclic ring comprises 1-3 heteroatoms independently selected from O, S, and N in the perimeter of the ring, where N may optionally be NR<sup>a</sup>, and S may optionally be SO or SO<sub>2</sub>;

R<sup>a</sup> and R<sup>b</sup> are independently selected from the group consisting of H, C<sub>1-5</sub>alkyl, C<sub>2-5</sub>alkenyl, C<sub>2-5</sub>alkynyl, -C(O)C<sub>1-5</sub>alkyl, -C(O)C<sub>2-5</sub>alkenyl, -C(O)C<sub>2-5</sub>alkynyl, SO<sub>x</sub>C<sub>1-5</sub>alkyl, SO<sub>x</sub>phenyl, SO<sub>x</sub>NR<sup>d</sup>R<sup>e</sup>, -C(O)NR<sup>d</sup>R<sup>e</sup>, halogen, and phenyl, wherein in all instances, alkyl, alkenyl, and alkynyl are linear or branched and are optionally substituted with (a) 1-5 halogen atoms, (b) 1-3 groups independently selected from -OCH<sub>3</sub>, -OCF<sub>3</sub> and phenyl, or (c) a mixture thereof, wherein phenyl in all

occurrences is optionally substituted with 1-3 substituents independently selected from halogen, C<sub>1</sub>-3alkyl, and C<sub>1</sub>-3alkoxy, said C<sub>1</sub>-3alkyl and C<sub>1</sub>-3alkoxy being linear or branched and optionally substituted with 1-5 halogens;

R<sup>d</sup> and R<sup>e</sup> are independently selected from H, C<sub>1</sub>-5alkyl, C<sub>2</sub>-5alkenyl, C<sub>2</sub>-5alkynyl, and phenyl, wherein said alkyl, alkenyl, and alkynyl are linear or branched and are optionally substituted with (a) 1-5 halogen atoms, (b) 1-3 groups independently selected from -OCH<sub>3</sub>, -OCF<sub>3</sub> and phenyl, or (c) a mixture thereof, wherein phenyl in all occurrences is optionally substituted with 1-3 substituents independently selected from halogen, C<sub>1</sub>-3alkyl, and C<sub>1</sub>-3alkoxy, said C<sub>1</sub>-3alkyl and C<sub>1</sub>-3alkoxy being linear or branched and optionally substituted with 1-5 halogens;

X and Y are independently selected from the group consisting of ~~O, S, SO, SO<sub>2</sub>, NR<sup>a</sup> and CH<sub>2</sub>~~; O and S;

n is an integer from 1-6;

R<sup>2</sup> is selected from the group consisting of Cl, Br, F and C<sub>1</sub>-4alkyl, wherein said C<sub>1</sub>-4alkyl is optionally substituted with 1-3 halogens; R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup> and R<sup>10</sup> are H;  
~~independently selected from the group consisting of H, halogen, C<sub>1</sub>-7alkyl, C<sub>2</sub>-7alkenyl, C<sub>2</sub>-7alkynyl, -OH, -OC<sub>1</sub>-5alkyl, -OC<sub>2</sub>-5alkenyl, -OC<sub>2</sub>-5alkynyl, -C(O)C<sub>1</sub>-5alkyl, -C(O)C<sub>2</sub>-5alkenyl, -C(O)C<sub>2</sub>-5alkynyl, -C(O)OC<sub>1</sub>-5alkyl, -C(O)OC<sub>2</sub>-5alkenyl, -C(O)OC<sub>2</sub>-5alkynyl, -OC(O)C<sub>1</sub>-5alkyl, -OC(O)C<sub>2</sub>-5alkenyl, -OC(O)C<sub>2</sub>-5alkynyl, Ar, OAr, C(O)Ar, C(O)OAr, OC(O)Ar, C<sub>3</sub>-8Cycloalkyl, -OC<sub>3</sub>-8Cycloalkyl, SO<sub>x</sub>C<sub>1</sub>-5alkyl, SO<sub>x</sub>NR<sup>a</sup>R<sup>b</sup>, SO<sub>x</sub>Ar, and -C(O)NR<sup>a</sup>R<sup>b</sup>, wherein in each instance, each alkyl, alkenyl, and alkynyl is linear or branched and is optionally substituted with (a) 1-5 halogen atoms, (b) 1-2 groups independently selected from -OC<sub>1</sub>-3alkyl groups which are linear or branched and are optionally substituted with 1-5 halogens, (c) 1 group Ar or C<sub>3</sub>-6Cycloalkyl, or (d) a mixture of more than one of (a), (b) and (c);~~

R<sup>4</sup> is selected from the group consisting of Benzoheterocycle, C<sub>3</sub>-8Cycloalkyl, Hetcyc, -OC<sub>3</sub>-8Cycloalkyl and RC, ~~with the proviso that if R<sup>4</sup> is R<sup>e</sup>, then either (1) R<sup>1</sup> is not H, and no more than one of R<sup>2</sup>, R<sup>6</sup>, and R<sup>10</sup> is alkyl, or (2) R<sup>2</sup> is Cl, Br or F, and R<sup>10</sup> is not alkyl;~~

wherein Benzoheterocycle, C<sub>3</sub>-8Cycloalkyl, Hetcyc and -OC<sub>3</sub>-8Cycloalkyl are each optionally substituted with 1-3 groups independently selected from halogen, C<sub>1</sub>-5alkyl, C<sub>2</sub>-5alkenyl,

C<sub>2</sub>-5alkynyl, -OC<sub>1</sub>-5alkyl, -OC<sub>2</sub>-5alkenyl, -OC<sub>2</sub>-5alkynyl, C<sub>3</sub>-8Cycloalkyl, -SO<sub>x</sub>C<sub>1</sub>-5alkyl, -SO<sub>x</sub>NR<sup>a</sup>R<sup>b</sup>, -SO<sub>x</sub>phenyl, C(O)C<sub>1</sub>-3alkyl and -C(O)NR<sup>a</sup>R<sup>b</sup>, wherein in all instances, said C<sub>1</sub>-5alkyl, C<sub>2</sub>-5alkenyl, and C<sub>2</sub>-5alkynyl groups are linear or branched and are optionally substituted with 1-3 halogens, and wherein Hetcyc, -OC<sub>3</sub>-8Cycloalkyl and C<sub>3</sub>-8Cycloalkyl may optionally have a C<sub>3</sub>-6-spiro-cycloalkyl substituent on the ring where gem-disubstitution of a ring carbon is possible, wherein the spiro-cycloalkyl group is optionally substituted with 1-2 groups independently selected from methyl, trifluoromethyl, methoxy, trifluoromethoxy and halogen;

wherein R<sup>c</sup> is selected from the group consisting of halogen, -OH, -OSO<sub>2</sub>C<sub>1</sub>-8alkyl, -OSO<sub>2</sub>C<sub>3</sub>-8Cycloalkyl, -OSO<sub>2</sub>Ar, C<sub>1</sub>-8alkyl, C<sub>2</sub>-8alkenyl, C<sub>2</sub>-8alkynyl, -OC<sub>1</sub>-8alkyl, -OC<sub>2</sub>-8alkenyl, -OC<sub>2</sub>-8alkynyl, and Aryl, wherein said -OSO<sub>2</sub>C<sub>1</sub>-8alkyl, C<sub>1</sub>-8alkyl, C<sub>2</sub>-8alkenyl, C<sub>2</sub>-8alkynyl, -OC<sub>1</sub>-8alkyl, -OC<sub>2</sub>-8alkenyl, and -OC<sub>2</sub>-8alkynyl are linear or branched, and are optionally substituted with (a) 1-5 halogens, (b) 1-2 groups independently selected from -OC<sub>1</sub>-3alkyl, which are linear or branched and which are optionally substituted with 1-5 halogens, (c) 1 group selected from Aryl and C<sub>3</sub>-8Cycloalkyl, or (d) a mixture of one or more of (a), (b) and (c), and Aryl and C<sub>3</sub>-8Cycloalkyl are each optionally substituted as defined under Ar for Aryl and R<sup>4</sup> for C<sub>3</sub>-8Cycloalkyl;

or alternatively R<sup>4</sup> and the adjacent substituent R<sup>3</sup> or R<sup>5</sup> may be connected to form a 5- or 6-membered heterocyclic ring that may be saturated, partly unsaturated or aromatic fused to the benzene ring, wherein the 5- or 6-membered fused ring comprises 1-3 heteroatoms independently selected from O, S, and N, where N may optionally be NR<sup>a</sup> and S may optionally be SO or SO<sub>2</sub>, said fused ring optionally also comprising 1-2 C=O groups in the perimeter of the ring, wherein said 5- or 6-membered heterocyclic fused ring is optionally substituted with 1-2 groups independently selected from R<sup>3</sup>.

2. (Cancelled)
3. (Original) A compound having formula I as recited in Claim 1, wherein X and Y are O.
4. (Original) A compound having formula I as recited in Claim 1, wherein Z is CH<sub>2</sub>.

5. (Original) A compound having formula I as recited in Claim 1, wherein Z is C=O.
6. (Original) A compound having formula I as recited in Claim 1, wherein n is 3 or 4.
7. (Cancelled)
8. (Cancelled)
9. (Original) A compound having formula I as recited in Claim 1, wherein the group -X- is attached to the benzopyran ring at the 6-position of the benzopyran ring.
10. (Original) A compound having formula I as recited in Claim 1, wherein the group -X- is attached to the benzopyran ring at the 7-position of the benzopyran ring.
11. (Original) A compound having formula I as recited in Claim 1, wherein R<sup>1</sup> is selected from a group consisting of C<sub>1-4</sub>alkyl, Cl and F, wherein alkyl is linear or branched and is optionally substituted with 1-5 F.
12. (Original) A compound as recited in claim 1, wherein Ar is phenyl, which is optionally substituted with 1-4 groups independently selected from Cl, F, C<sub>1-5</sub>alkyl, -OCH<sub>3</sub>, -OCF<sub>3</sub>, -SO<sub>x</sub>C<sub>1-5</sub>alkyl, -SO<sub>x</sub>NR<sub>a</sub>R<sub>b</sub>, -SO<sub>x</sub>phenyl, -C(O)C<sub>1-3</sub>alkyl, and -C(O)NR<sub>a</sub>R<sub>b</sub>, wherein phenyl of -SO<sub>x</sub>phenyl is optionally substituted with 1-3 substituents independently selected from halogen, CH<sub>3</sub>, CF<sub>3</sub>, -OCF<sub>3</sub>, and -OCH<sub>3</sub>, and wherein alkyl in all occurrences is linear or branched and is optionally substituted with 1-5 halogens.
13. (Currently Amended) A compound as recited in claim 1, wherein R<sup>1</sup> and R<sup>2</sup> are each independently selected from a group consisting of C<sub>1-4</sub>alkyl, Cl and F; n is 2-4; X and Y are O; Z is CH<sub>2</sub>; ~~R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup> and R<sup>10</sup> are independently selected from H, Cl, F, CH<sub>3</sub> and CF<sub>3</sub>~~; and in all occurrences, alkyl is linear or branched and is optionally substituted with 1-5 F.

14. (Currently Amended) A compound having formula I as recited in Claim 1, wherein ~~R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, and R<sup>10</sup> are H~~; R<sup>2</sup> is Cl or F; and R<sup>1</sup> is C<sub>1</sub>-4alkyl, Cl or F, where C<sub>1</sub>-4alkyl is linear or branched and is optionally substituted with 1-5 F.

15. (Cancelled)

16. (Original) A compound as recited in Claim 1, wherein R<sup>a</sup> and R<sup>b</sup> are independently selected from the group consisting of H, C<sub>1</sub>-5alkyl, -C(O)C<sub>1</sub>-5alkyl, S(O)<sub>x</sub>C<sub>1</sub>-5alkyl, S(O)<sub>x</sub>phenyl, and phenyl, wherein alkyl in all occurrences is linear or branched and is optionally substituted with 1-5 halogen atoms, and wherein phenyl in all occurrences is optionally substituted with 1-3 substituents independently selected from halogen, C<sub>1</sub>-3alkyl, and C<sub>1</sub>-3alkoxy, wherein C<sub>1</sub>-3alkyl and C<sub>1</sub>-3alkoxy are linear or branched and are optionally substituted with 1-5 halogens.

17. (Cancelled)

18. (Currently Amended) A compound as recited in Claim 1, wherein R<sup>4</sup> is R<sup>c</sup>, and R<sup>2</sup> is Cl, Br or F, ~~with the proviso that R<sup>10</sup> is not alkyl~~.

19. (Original) A compound having Formula I as recited in Claim 1, wherein R<sup>4</sup> is joined to R<sup>3</sup> or to R<sup>5</sup> to yield a benzoheterocycle which comprises a 5 or 6-membered heterocyclic ring which may be saturated, partly unsaturated or aromatic fused to the benzene ring, wherein said benzoheterocycle is selected from the group consisting of benzoxazole, benzisoxazole, benzofuran, indole, benzothiophene, benzthiazole, benzodiazene, quinazoline, benzoxazine, benzisoxazine, benzimidazole, and benzpyrazole, wherein said benzoheterocycle is optionally substituted on the heterocyclic ring with 1-2 groups independently selected from halogen, phenyl, C<sub>1</sub>-4alkyl, and -OC<sub>1</sub>-4alkyl, wherein C<sub>1</sub>-4alkyl and -OC<sub>1</sub>-4alkyl are linear or branched and are optionally substituted with 1-5 halogens, and said phenyl is optionally substituted with 1-5 substituents independently selected from halogen, C<sub>1</sub>-3alkyl and C<sub>1</sub>-3alkoxy groups, wherein the C<sub>1</sub>-3alkyl and C<sub>1</sub>-3alkoxy groups are linear or branched and are optionally substituted with 1-5 halogens.

20. (Original) A compound having formula I as recited in Claim 19, wherein R<sup>4</sup> and R<sup>3</sup> or R<sup>5</sup> are joined together to form a benzisoxazole ring, which is optionally substituted on the

isoxazole ring with 1 group selected from C<sub>1-4</sub>alkyl and phenyl, wherein C<sub>1-4</sub>alkyl is linear or branched and is optionally substituted with (a) 1-3 halogens, (b) 1 phenyl, or (c) a mixture of (a) and (b); and phenyl in all occurrences is optionally substituted with 1-3 groups independently selected from halogen, C<sub>1-3</sub>alkyl and -OC<sub>1-3</sub>alkyl, wherein said C<sub>1-3</sub>alkyl and -OC<sub>1-3</sub>alkyl are linear or branched and are optionally substituted with 1-3 halogens.

21. (Original) A compound having Formula I as recited in Claim 1, wherein R<sup>4</sup> is selected from the group consisting of C<sub>3-8</sub>Cycloalkyl and Hetcyc, each of which is optionally substituted with 1-4 substituents independently selected from halogen, phenyl, C<sub>1-5</sub>alkyl, and -OC<sub>1-5</sub>alkyl, wherein C<sub>1-5</sub>alkyl and -OC<sub>1-5</sub>alkyl are linear or branched and are optionally substituted with 1-5 halogens, and phenyl is optionally substituted with 1-5 substituents independently selected from halogen, C<sub>1-3</sub>alkyl and -OC<sub>1-3</sub>alkyl, wherein C<sub>1-3</sub>alkyl and -OC<sub>1-3</sub>alkyl are linear or branched and are optionally substituted with 1-5 halogens, and wherein two substituents on the same carbon of said C<sub>3-8</sub>Cycloalkyl and Hetcyc may optionally join together to form a C<sub>3-6</sub>-spiro-cycloalkyl group, wherein the spiro-cycloalkyl group is optionally substituted with 1-2 groups independently selected from methyl, trifluoromethyl, methoxy, trifluoromethoxy and halogen.

22. (Original) A compound having Formula I as recited in Claim 21, wherein R<sup>4</sup> is Hetcyc or C<sub>3-6</sub>Cycloalkyl, wherein Hetcyc is a saturated heterocyclic compound having 1-2 heteroatoms in the perimeter of the ring and is otherwise as defined in Claim 1, and C<sub>3-6</sub>Cycloalkyl is a saturated 3-6-membered cycloalkyl, wherein Hetcyc and C<sub>3-6</sub>Cycloalkyl optionally have 1-2 substituents independently selected from halogen, C<sub>1-3</sub>alkyl and C<sub>2-3</sub>alkenyl, wherein said C<sub>1-3</sub>alkyl and C<sub>2-3</sub>alkenyl are linear or branched and are optionally substituted with 1-3 halogens, or alternatively two substituents may be joined on one carbon atom of the ring to form a spiro-cycloalkyl group having 3-6 carbons.

23. (Original) A compound having formula I as recited in Claim 22, wherein R<sup>4</sup> is selected from piperidine, 1,4-dioxane, tetrahydropyran, piperazine, morpholine, cyclohexane, cyclopentane, cyclobutane and cyclopropane, wherein R<sup>4</sup> is optionally substituted as defined in Claim 22.

24. (Original) A compound having formula I as recited in Claim 23, wherein R<sup>4</sup> is R<sup>C</sup> and is selected from the group consisting of halogen, C<sub>1</sub>-galkyl, C<sub>2</sub>-galkenyl, C<sub>2</sub>-galkynyl, -OC<sub>1</sub>-galkyl, -OC<sub>2</sub>-galkenyl, -OC<sub>2</sub>-galkynyl, and Aryl, wherein C<sub>1</sub>-galkyl, C<sub>2</sub>-galkenyl, C<sub>2</sub>-galkynyl, -OC<sub>1</sub>-galkyl, -OC<sub>2</sub>-galkenyl, and -OC<sub>2</sub>-galkynyl are linear or branched, and are optionally substituted with (a) 1-5 halogens, (b) 1-2 groups independently selected from -OC<sub>1</sub>-3alkyl, which are linear or branched and which are optionally substituted with 1-5 halogens, (c) 1 group Aryl or C<sub>3</sub>-6Cycloalkyl, or (d) a mixture of more than one of (a), (b) and (c), wherein Aryl and C<sub>3</sub>-6Cycloalkyl are optionally substituted with 1-3 substituents independently selected from halogen, C<sub>1</sub>-3alkyl and -OC<sub>1</sub>-3alkyl, said C<sub>1</sub>-3alkyl and -OC<sub>1</sub>-3alkyl being linear or branched and optionally substituted with 1-5 halogens, phenyl or C<sub>3</sub>-6Cycloalkyl.

25. (Original) A compound having formula I as recited in Claim 24, wherein R<sup>4</sup> is selected from the group consisting of C<sub>1</sub>-4alkyl and -OC<sub>1</sub>-4alkyl, wherein said C<sub>1</sub>-4alkyl and -OC<sub>1</sub>-4alkyl are linear or branched and are optionally substituted with one C<sub>3</sub>-6Cycloalkyl group, 1-5 halogens independently selected from Cl and F, or a mixture of both.

26. (Currently Amended) A compound having formula I as recited in Claim 24, wherein Aryl is phenyl; R<sup>1</sup> is selected from a group consisting of C<sub>1</sub>-4alkyl, Cl and F, wherein alkyl is linear or branched and is optionally substituted with 1-5 F; and R<sup>2</sup> is selected from Cl and F; ~~and R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, and R<sup>10</sup> are independently selected from H, CH<sub>3</sub>, CF<sub>3</sub>, Cl and F.~~

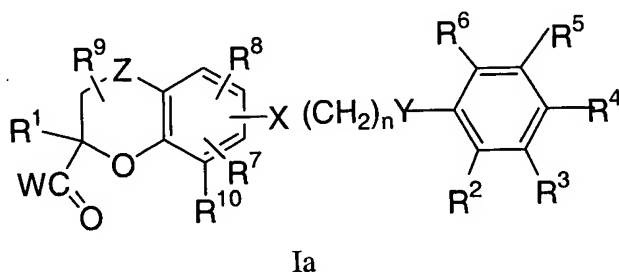
27. (Currently Amended) A compound having formula I as recited in Claim 1, wherein ~~R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, and R<sup>10</sup> are H~~; R<sup>1</sup> is C<sub>1</sub>-4alkyl, Cl or F; and R<sup>2</sup> is Cl or F.

28. (Currently Amended) A compound having formula I as recited in Claim 1, wherein R<sup>1</sup> is selected from linear or branched C<sub>1</sub>-4 alkyl, Cl and F; R<sup>2</sup> is Cl or F; ~~R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup> and R<sup>10</sup> are each H~~; Z is CH<sub>2</sub>; ~~X and Y are O or S~~; and R<sup>4</sup> is selected from halogen, phenyl, C<sub>1</sub>-galkyl, -OC<sub>1</sub>-galkyl, C<sub>3</sub>-6Cycloalkyl, and tetrahydropyran, wherein said C<sub>1</sub>-galkyl and -OC<sub>1</sub>-galkyl groups are linear or branched and are optionally substituted with (a) 1-5 halogen atoms, (b) 1 group selected from phenyl, C<sub>3</sub>-6Cycloalkyl, and linear or branched -OC<sub>1</sub>-3alkyl optionally substituted with 1-5 halogens, or (c) a mixture of (a) and (b), and wherein said phenyl, C<sub>3</sub>-6Cycloalkyl and



tetrahydropyran groups are optionally substituted with 1-2 groups independently selected from halogen, -OCH<sub>3</sub>, -CH<sub>3</sub>, -OCF<sub>3</sub>, and -CF<sub>3</sub>.

29. (Currently Amended) A compound having formula Ia:



or a pharmaceutically acceptable salt or metabolite thereof, wherein ~~W is a group that is easily removed under physiological conditions during or after administration to a mammalian patient to yield a carboxylic acid in which W is OH, or the carboxylate anion thereof, or a pharmaceutically acceptable salt thereof, and R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup>, Ar, X, Y, Z, R<sup>a</sup>, R<sup>b</sup>, R<sup>d</sup>, R<sup>e</sup>, x and n are as defined in Claim 1.~~

W is selected from the group consisting of -OR<sup>13</sup>, -OCH<sub>2</sub>OR<sup>13</sup>, -OCH(CH<sub>3</sub>)OR<sup>13</sup>, -OCH<sub>2</sub>OC(O)R<sup>13</sup>, -OCH(CH<sub>3</sub>)OC(O)R<sup>13</sup>, -OCH<sub>2</sub>OC(O)OR<sup>13</sup>, -OCH(CH<sub>3</sub>)OC(O)OR<sup>13</sup>, and -NR<sup>14</sup>R<sup>14</sup>, wherein each R<sup>13</sup> is independently selected from C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one or two groups independently selected from -CO<sub>2</sub>H, -CONH<sub>2</sub>, NH<sub>2</sub>, -OH, -OAc, NHAc and phenyl; and wherein each R<sup>14</sup> is independently selected from H and R<sup>13</sup>; wherein

Z is selected from the group consisting of CH<sub>2</sub> and C=O;

R<sup>1</sup> is selected from the group consisting of Cl, Br, F and C<sub>1</sub>-4 alkyl, wherein said C<sub>1</sub>-4 alkyl is linear or branched and is optionally substituted with 1-3 halogens independently selected from F and Cl, 1 phenyl which is optionally substituted with 1-3 halogens, or a mixture thereof;

Ar is Aryl, wherein Aryl is in each instance optionally substituted with 1-5 substituents independently selected from (a) halogen, (b) C<sub>1</sub>-5 alkyl, (c) C<sub>2</sub>-5 alkenyl, (d) C<sub>2</sub>-5 alkynyl, (e) -OC<sub>1</sub>-5 alkyl, (f) -OC<sub>2</sub>-5 alkenyl, (g) -OC<sub>2</sub>-5 alkynyl, (h) -SO<sub>x</sub>C<sub>1</sub>-5 alkyl, (i) -SO<sub>x</sub>NR<sup>a</sup>R<sup>b</sup>, (j) -SO<sub>x</sub>phenyl, (k)

-C(O)C<sub>1-3</sub>alkyl, and (l) -C(O)NR<sup>a</sup>R<sup>b</sup>, wherein in each instance, each alkyl, alkenyl and alkynyl is linear or branched and is optionally substituted with (a) 1-5 halogen atoms, (b) 1-2 groups independently selected from -OC<sub>1-3</sub>alkyl, which is linear or branched and is optionally substituted with 1-5 halogens, or (c) a mixture thereof, and wherein phenyl is optionally substituted with 1-3 substituents independently selected from halogen, C<sub>1-3</sub>alkyl, and C<sub>1-3</sub>alkoxy, wherein C<sub>1-3</sub>alkyl and C<sub>1-3</sub>alkoxy are linear or branched and are optionally substituted with 1-5 halogens;

x is selected from 0, 1 and 2;

Aryl is a carbocyclic 6-10 membered monocyclic or bicyclic aromatic ring system;

Hetcyc is a 5- or 6-membered saturated or partly saturated monocyclic heterocycle having 1-4 heteroatoms independently selected from N, S, and O in the perimeter of the ring, wherein N may optionally be NR<sup>a</sup> and S may optionally be SO or SO<sub>2</sub>;

Benzoheterocycle comprises a 5 or 6-membered heterocyclic ring which may be saturated, partly unsaturated or aromatic, and a benzene ring, wherein said heterocyclic ring and said benzene ring are fused together, wherein said heterocyclic ring comprises 1-3 heteroatoms independently selected from O, S, and N in the perimeter of the ring, where N may optionally be NR<sup>a</sup>, and S may optionally be SO or SO<sub>2</sub>;

R<sup>a</sup> and R<sup>b</sup> are independently selected from the group consisting of H, C<sub>1-5</sub>alkyl, C<sub>2-5</sub>alkenyl, C<sub>2-5</sub>alkynyl, -C(O)C<sub>1-5</sub>alkyl, -C(O)C<sub>2-5</sub>alkenyl, -C(O)C<sub>2-5</sub>alkynyl, SO<sub>x</sub>C<sub>1-5</sub>alkyl, SO<sub>x</sub>phenyl, SO<sub>x</sub>NR<sup>d</sup>Re, -C(O)NR<sup>d</sup>Re, halogen, and phenyl, wherein in all instances, alkyl, alkenyl, and alkynyl are linear or branched and are optionally substituted with (a) 1-5 halogen atoms, (b) 1-3 groups independently selected from -OCH<sub>3</sub>, -OCF<sub>3</sub>, and phenyl, or (c) a mixture thereof, wherein phenyl in all occurrences is optionally substituted with 1-3 substituents independently selected from halogen, C<sub>1-3</sub>alkyl, and C<sub>1-3</sub>alkoxy, said C<sub>1-3</sub>alkyl and C<sub>1-3</sub>alkoxy being linear or branched and optionally substituted with 1-5 halogens;

R<sup>d</sup> and R<sup>e</sup> are independently selected from H, C<sub>1-5</sub>alkyl, C<sub>2-5</sub>alkenyl, C<sub>2-5</sub>alkynyl, and phenyl, wherein said alkyl, alkenyl, and alkynyl are linear or branched and are optionally substituted

with (a) 1-5 halogen atoms, (b) 1-3 groups independently selected from -OCH<sub>3</sub>, -OCF<sub>3</sub> and phenyl, or (c) a mixture thereof, wherein phenyl in all occurrences is optionally substituted with 1-3 substituents independently selected from halogen, C<sub>1-3</sub>alkyl, and C<sub>1-3</sub>alkoxy, said C<sub>1-3</sub>alkyl and C<sub>1-3</sub>alkoxy being linear or branched and optionally substituted with 1-5 halogens;

X and Y are independently selected from the group consisting of O and S;

n is an integer from 1-6;

R<sup>2</sup> is selected from the group consisting of Cl, Br, F and C<sub>1-4</sub>alkyl, wherein said C<sub>1-4</sub>alkyl is optionally substituted with 1-3 halogens;

R<sup>4</sup> is selected from the group consisting of Benzoheterocycle, C<sub>3-8</sub>Cycloalkyl, Hetcyc, -OC<sub>3-8</sub>Cycloalkyl and R<sup>c</sup>;

wherein Benzoheterocycle, C<sub>3-8</sub>Cycloalkyl, Hetcyc and -OC<sub>3-8</sub>Cycloalkyl are each optionally substituted with 1-3 groups independently selected from halogen, C<sub>1-5</sub>alkyl, C<sub>2-5</sub>alkenyl, C<sub>2-5</sub>alkynyl, -OC<sub>1-5</sub>alkyl, -OC<sub>2-5</sub>alkenyl, -OC<sub>2-5</sub>alkynyl, C<sub>3-8</sub>Cycloalkyl, -SO<sub>x</sub>C<sub>1-5</sub>alkyl, -SO<sub>x</sub>NR<sup>a</sup>R<sup>b</sup>, -SO<sub>x</sub>phenyl, C(O)C<sub>1-3</sub>alkyl and -C(O)NR<sup>a</sup>R<sup>b</sup>, wherein in all instances, said C<sub>1-5</sub>alkyl, C<sub>2-5</sub>alkenyl, and C<sub>2-5</sub>alkynyl groups are linear or branched and are optionally substituted with 1-3 halogens, and wherein Hetcyc, -OC<sub>3-8</sub>Cycloalkyl and C<sub>3-8</sub>Cycloalkyl may optionally have a C<sub>3-6</sub>-spiro-cycloalkyl substituent on the ring where gem-disubstitution of a ring carbon is possible, wherein the spiro-cycloalkyl group is optionally substituted with 1-2 groups independently selected from methyl, trifluoromethyl, methoxy, trifluoromethoxy and halogen;

wherein R<sup>c</sup> is selected from the group consisting of halogen, -OH, -OSO<sub>2</sub>C<sub>1-8</sub>alkyl, -OSO<sub>2</sub>C<sub>3-8</sub>Cycloalkyl, -OSO<sub>2</sub>Ar, C<sub>1-8</sub>alkyl, C<sub>2-8</sub>alkenyl, C<sub>2-8</sub>alkynyl, -OC<sub>1-8</sub>alkyl, -OC<sub>2-8</sub>alkenyl, -OC<sub>2-8</sub>alkynyl, and Aryl, wherein said -OSO<sub>2</sub>C<sub>1-8</sub>alkyl, C<sub>1-8</sub>alkyl, C<sub>2-8</sub>alkenyl, C<sub>2-8</sub>alkynyl, -OC<sub>1-8</sub>alkyl, -OC<sub>2-8</sub>alkenyl, and -OC<sub>2-8</sub>alkynyl are linear or branched, and are optionally substituted with (a) 1-5 halogens, (b) 1-2 groups independently selected from -OC<sub>1-3</sub>alkyl, which are linear or branched and which are optionally substituted with 1-5 halogens, (c) 1 group selected from Aryl and C<sub>3-8</sub>Cycloalkyl, or (d) a mixture of one or more of (a), (b) and (c), and Aryl and C<sub>3-8</sub>Cycloalkyl are each optionally substituted as defined under Ar for Aryl and R<sup>4</sup> for C<sub>3-8</sub>Cycloalkyl;

or alternatively R<sup>4</sup> and the adjacent substituent R<sup>3</sup> or R<sup>5</sup> may be connected to form a 5- or 6-membered heterocyclic ring that may be saturated, partly unsaturated or aromatic fused to the benzene ring, wherein the 5- or 6-membered fused ring comprises 1-3 heteroatoms independently selected from O, S, and N, where N may optionally be NR<sup>a</sup> and S may optionally be SO or SO<sub>2</sub>, said fused ring optionally also comprising 1-2 C=O groups in the perimeter of the ring, wherein said 5- or 6-membered heterocyclic fused ring is optionally substituted with 1-2 groups independently selected from R<sup>3</sup>.

30. (Cancelled)

31. (Previously Presented) A compound as recited in Claim 1, wherein the stereochemistry at the 2-position of the benzopyranyl ring is R.

32. (Previously Presented) A compound as recited in Claim 1, wherein the stereochemistry at the 2-position of the benzopyranyl ring is S.

33. (Cancelled)

34. (Cancelled)

35. (Previously Presented) A pharmaceutical composition comprising a compound as identified in Claim 1 and a pharmaceutically acceptable carrier.

36. (Previously Presented) A method for treating or controlling non-insulin dependent (Type 2) diabetes mellitus in a mammalian patient in need of such treatment which comprises administering to said patient a therapeutically effective amount of a compound of Claim 1.

37. (Previously Presented) A method for treating or controlling hyperglycemia in a mammalian patient in need of such treatment which comprises administering to said patient a therapeutically effective amount of a compound of Claim 1.

38. (Previously Presented) A method for treating or controlling lipid disorders, hyperlipidemia, or low HDL in a mammalian patient in need of such treatment which comprises administering to said patient a therapeutically effective amount of a compound of Claim 1.

39. (Previously Presented) A method for treating or controlling obesity in a mammalian patient in need of such treatment which comprises administering to said patient a therapeutically effective amount of a compound of Claim 1.

40. (Previously Presented) A method for treating or controlling hypercholesterolemia in a mammalian patient in need of such treatment which comprises administering to said patient a therapeutically effective amount of a compound of Claim 1.

41. (Previously Presented) A method for treating or controlling hypertriglyceridemia in a mammalian patient in need of such treatment which comprises administering to said patient a therapeutically effective amount of a compound of Claim 1.

42. (Previously Presented) A method for treating or controlling dyslipidemia and/or low HDL cholesterol in a mammalian patient in need of such treatment which comprises administering to said patient a therapeutically effective amount of a compound of Claim 1.

43. (Previously Presented) A method for treating or controlling atherosclerosis in a mammalian patient in need of such treatment which comprises administering to said patient a therapeutically effective amount of a compound of Claim 1.

44. (Previously Presented) A method for treating or controlling cachexia in a mammalian patient in need of such treatment which comprises administering to said patient a therapeutically effective amount of a compound of Claim 1.

45. (Previously Presented) A method of treating or controlling one or more diseases, disorders, or conditions selected from the group consisting of (1) non-insulin dependent diabetes mellitus (NIDDM), (2) hyperglycemia, (3) impaired glucose tolerance, (4) insulin resistance, (5) obesity, (6) lipid disorders, (7) dyslipidemia, (8) hyperlipidemia, (9) hypertriglyceridemia, (10) hypercholesterolemia, (11) low HDL levels, (12) high LDL levels, (13) atherosclerosis and its sequelae, (14) vascular restenosis, (15) irritable bowel syndrome, (16) inflammatory bowel disease, including Crohn's disease and ulcerative colitis, (17) other inflammatory conditions, (18) pancreatitis, (19) abdominal obesity, (20) neurodegenerative disease, (21) retinopathy, (22) neoplastic conditions, (23) adipose cell tumors, (24) adipose cell carcinomas, such as liposarcoma, (25) prostate cancer and other cancers, including gastric, breast, bladder and colon cancers, (26) angiogenesis, (27) Alzheimer's disease, (28) psoriasis, (29) acne vulgaris, (30) skin diseases modulated by PPAR, (31) high blood pressure, (32) Syndrome X, (33) ovarian hyperandrogenism (polycystic ovarian syndrome), and other disorders where insulin resistance is a component, said method comprising the administration of an effective amount of a compound of Claim 1.

46. (Previously Presented) A method of treating or controlling one or more diseases, disorders, or conditions selected from the group consisting of (1) diabetes mellitus, and non-insulin dependent diabetes mellitus (NIDDM), (2) hyperglycemia, (3) impaired glucose tolerance, (4) insulin resistance, (5) obesity, (6) lipid disorders, (7) dyslipidemia, (8) hyperlipidemia, (9) hypertriglyceridemia, (10) hypercholesterolemia, (11) low HDL levels, (12) high LDL levels, (13) atherosclerosis and its sequelae, (14) vascular restenosis, (15) irritable bowel syndrome, (16) inflammatory bowel disease, including Crohn's disease and ulcerative colitis, (17) other inflammatory conditions, (18) pancreatitis, (19) abdominal obesity, (20) neurodegenerative disease, (21) retinopathy, (22) neoplastic conditions, (23) adipose cell tumors, (24) adipose cell carcinomas, such as liposarcoma, (25) prostate cancer and other cancers, including gastric, breast, bladder and colon cancers, (26) angiogenesis, (27) Alzheimer's disease, (28) psoriasis, (29) acne vulgaris, (30) skin diseases modulated by PPAR, (31) high blood pressure, (32) Syndrome X, (33) ovarian hyperandrogenism (polycystic ovarian syndrome), and other disorders where insulin resistance is a component, said method comprising the administration of an effective amount of a compound of Claim 1, and an effective amount of one or more other compounds selected from the group consisting of:

(a) insulin sensitizers; (i) PPAR $\gamma$  agonists; (ii) biguanides; (iii) protein tyrosine phosphatase-1B (PTP-1B) inhibitors; (iv) dipeptidyl peptidase IV inhibitors;

(b) insulin or insulin mimetics;

(c) sulfonylureas;

(d)  $\alpha$ -glucosidase inhibitors;

(e) cholesterol lowering agents selected from the group consisting of (i) HMG-CoA reductase inhibitors, (ii) sequestrants, (iii) nicotiny alcohol, nicotinic acid or a salt thereof, (iv) PPAR $\alpha$  agonists, (v) PPAR $\alpha$ / $\gamma$  dual agonists, (vi) inhibitors of cholesterol absorption, (vii) acyl CoA:cholesterol acyltransferase inhibitors, and (viii) anti-oxidants;

(f) PPAR $\delta$  agonists;

(g) antiobesity compounds (anorectics);

(h) an ileal bile acid transporter inhibitor; and

(i) anti-inflammatory agents.

47. (Previously Presented) A method for the treatment or control of one or more conditions selected from hypercholesterolemia, atherosclerosis, low HDL levels, high LDL levels, hyperlipidemia, hypertriglyceridemia, and dyslipidemia, which method comprises administering to a mammalian patient in need of such treatment a therapeutically effective amount of a compound of Claim 1 and a therapeutically effective amount of an HMG-CoA reductase inhibitor.

48. (Original) The method as recited in Claim 47, wherein the HMG-CoA reductase inhibitor is a statin.

49. (Previously Presented) The method as recited in Claim 48, wherein the statin is selected from the group consisting of lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin, itavastatin, rosuvastatin and rivastatin.

50. (Previously Presented) A method for the treatment or control of one or more conditions selected from inflammatory conditions, inflammatory bowel disease, Crohn's disease, and ulcerative colitis, which method comprises administering to a mammalian patient in need of such treatment a therapeutically effective amount of a compound according to Claim 1.

51. (Previously Presented) A method for treating or preventing atherosclerosis in a mammalian patient in need of such treatment comprising the administration to said patient of an

effective amount of a compound of Claim 1 and an effective amount of an HMG-CoA reductase inhibitor.

52. (Original) The method as recited in Claim 51, wherein the HMG-CoA reductase inhibitor is a statin.

53. (Previously Presented) The method as recited in Claim 52, wherein the statin is selected from the group consisting of lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin, itavastatin, rosuvastatin and rivastatin.

54. (Previously Presented) A pharmaceutical composition comprising: (1) a compound according to Claim 1, (2) an HMG-CoA reductase inhibitor, and (3) a pharmaceutically acceptable carrier.

55. (Previously Presented) A pharmaceutical composition comprising (1) a compound according to Claim 1, (2) one or more compounds selected from the group consisting of :

- (a) insulin sensitizers; (ii) biguanides; (I) PPAR $\gamma$  agonists; (iii) protein tyrosine phosphatase-1B (PTP-1B) inhibitors, and (iv) dipeptidyl peptidase IV (DP-IV) inhibitors;
  - (b) insulin or insulin mimetics;
  - (c) sulfonylureas;
  - (d)  $\alpha$ -glucosidase inhibitors;
  - (e) cholesterol lowering agents selected from the group consisting of (i) HMG-CoA reductase inhibitors, (ii) sequestrants, (iii) nicotiny alcohol, nicotinic acid or a salt thereof, (iv) PPAR $\alpha$  agonists, (v) PPAR $\alpha$ / $\gamma$ dual agonists, (vi) inhibitors of cholesterol absorption, (vii) acyl CoA:cholesterol acyltransferase inhibitors, and (viii) anti-oxidants;
  - (f) PPAR $\delta$  agonists;
  - (g) antiobesity compounds (anorectics);
  - (h) an ileal bile acid transporter inhibitor; and
  - (i) anti-inflammatory agents; and
- (3) a pharmaceutically acceptable carrier.



56. (Previously Presented) A compound represented by a structure shown below, or a pharmaceutically acceptable salt or prodrug thereof, wherein the structure is selected from the group consisting of:

